REPORT OF THE

ENVIRONMENTAL HYPERSENSITIVITY ADVISORY COMMITTEE

TO THE

MINISTER OF HEALTH
PROVINCE OF NOVA SCOTIA

December 18, 1986

Nova Scotia

G. Ross Langley, M.D., F.R.C.P.(C), F.A.C.P., F.R.C.P. (Edin.)
Division of Hematology/Medical Oncology
Room 4194, Victoria General Hospital, Halifax, N. S., B3H 2Y9
Telephone: 428-2107 Pager 428-3801 #9115

Victoria General Hospital

1278 Tower Road
Halifax, Nova Scotia
B3H 2Y9

January 7, 1987

Honourable Ronald S. Russell
Minister of Health
Department of Health
Joseph Howe Building
690 Hollis Street
Halifax, Nova Scotia

Dear Mr. Russell:

The Advisory Committee on Environmental Hypersensitivity has completed its work on this subject and is pleased to submit the attached report for your consideration.

Yours very truly,

*
Dr. J. Patricia Beresford

Dr. Thomas J. Marrie

Dr. John G.Gatien

Dr. J. Michael MacSween

Dr. G. Ross Langley (Chair)

Dr. John T. Sears

Dr. Dianne D. MacDonald

/sma

* Dr. P. Beresford will submit a separate report.

REPORT OF THE

ENVIRONMENTAL HYPERSENSITIVITY ADVISORY COMMITTEE

TO THE

MINISTER OF HEALTH
PROVINCE OF NOVA SCOTIA

December 18, 1986

I. INTRODUCTION

II. BACKGROUND ON ENVIRONMENTAL HYPERSENSITIVITY

A. Environmental Hypersensitivity in Nova Scotia
B. Allergy and Hypersensitivity
C. Occupational Medicine and Toxicology
D. Post Infection Syndromes
E. Fibrositis and Fibromyalgia
F. Total Allergy Syndrome, Twentieth Century Disease, Environmental Hypersensitivity; Clinical Ecology

III. CAUSAL INFERENCES

IV. ADVISORY COMMITTEE ON "ENVIRONMENTAL HYPERSENSITIVITY"

A. Current Concepts in the Theory, and the Diagnosis and Treatment of "Environmental Hypersensitivity".
B. Medical Aspects of "Environmental Hypersensitivity" in Nova Scotia.
C. Patient Concerns and the Recommendations of the Allergy and Environmental Hypersensitivity Society of Nova Scotia.

V. CONCLUSIONS AND RECOMMENDATIONS

A) SOME COMMENTS ON RELATED ISSUES

1. Relationship between "allergy" and "environmental hypersensitivity".
2. Relationship between environmental "toxicity" and "sensitivity".
3. Is there a mechanism to explain the production of such diverse symptoms?
4. Is there a causal relationship between exposure and symptoms?
5. Are there other explanations for the symptoms?
6. Regardless of causation should environmental manipulation be encouraged?

B) RESPONSE TO THE SPECIFIC QUESTIONS IN THE TERMS OF REFERENCE

1. Is there an identifiable condition known as Environmental Hypersensitivity, Twentieth Century Disease or Total Allergy Syndrome?
2. Are any additional diagnostic or therapeutic services required in Nova Scotia to help patients and their physicians who believe they may be suffering from this condition?
3. Is there a medical necessity to refer these patients to a center outside Nova Scotia or Canada for treatment?
4. If so, what should be the appropriate procedures by which the cases of patients who believe themselves to be suffering from environmental hypersensitivity should be reviewed in the event that a request to approve an out-of-country referral is received by the Department of Health?

VI. Summary

I. INTRODUCTION:

The Environmental Hypersensitivity Advisory Committee to the Minister of Health was appointed by the Minister in May 1986 with members selected from nominees put forward by the Nova Scotia Medical Society, the Faculty of Medicine, Dalhousie University, the Provincial Medical Board of Nova Scotia, The Department of Health and the Allergy and Environmental Sensitivity Society of Nova Scotia. The Committee consisted of Dr. J. Patricia Beresford, Dr. John G. Gatien, Dr. G. Ross Langley (Chair), Dr. Thomas J. Marrie, Dr. Dianne D. MacDonald, Dr. J. Michael MacSween and Dr. John T. Sears. Dr. Alan D. Thomson, Administrator, Health Care Institutions for the Province of Nova Scotia and Dr. Douglas W. Archibald, Administrator, Psychiatric Mental Health Services for the Province, were observers at the Committee's meetings. The Committee's terms of reference listed four functions.

1. To advise the Minister whether or not there is an identifiable condition known as environmental hypersensitivity or twentieth century disease or total allergy syndrome.

2. To advise the Minister of any additional diagnostic or therapeutic services that may be required in Nova Scotia to help patients and their physicians who believe they may be suffering from this condition.

3. Provide an opinion as to the medical necessity of referring these patients to a center outside Nova Scotia or Canada for diagnosis and/or treatment.

4. To advise the Minister on the appropriate procedures by which the cases of patients who believe themselves to be suffering from environmental hypersensitivity should be reviewed, in the event that a request to approve an out-of-country referral is received by the Department of Health.

The Committee began the study of this subject immediately after being appointed and held its first meeting on May 23, 1986. It met about once weekly throughout the summer and concluded its study, following a visit to an out of country environmental health unit, in December 1986.

II. BACKGROUND ON "ENVIRONMENTAL HYPERSENSITIVITY"

a) Environmental Hypersensitivity in Nova Scotia:

In 1984 the Department of Health received a request from a specialist in Internal Medicine in Halifax for the referrral of a patient to the Environmental Health Clinic in Dallas, Texas. The Department gave approval for this referral on the understanding that this was for a two week period and that all results would be available for study by medical people. Following the patient's four week stay at the Environmental Health Clinic the results were reviewed by an Ad Hoc Committee convened by the Department of Health for that purpose. The Ad Hoc Committee consisted of an

allergist, immunologist, general internal medicine specialist, psychiatrist and the patient's family physician. From this review the Ad Hoc Committee concluded that there was no indication of allergy in the patient's symptoms and that alternate explanations for these should be explored. Subsequently additional requests have been received by the Department of Health for referral of patients to out of country facilities for investigation of "environmental hypersensitivity". All these requests were reviewed by Ad Hoc Committees convened for these specific purposes. These requests and the knowledge that a Society for Allergy and Environmental Hypersensitivity had been formed in the Province led the Minister of Health to request a review of this subject so as to develop an appropriate Nova Scotia policy.

Before proceeding to discuss "environmental hypersensitivity" the Committee will review four clinical subjects (see Sections IIb, IIc, IId, IIe), which we think provide important background information necessary to an understanding of "Environmental Hypersensitivity", Twentieth Century Disease", "Total Allergy Syndrome".

b) Allergy and Hypersensitivity:

Allergy is a word that is frequently used in the practice of medicine and also by the general public. As a medical word allergy has a specific meaning. The term was suggested by vonPirquet in the early 1900's to describe the altered response observed in organisms and tissues to repeated contacts with virus, tuberculin, and foreign serums. In the ensuing eighty years much has been learned about allergy and its effects on humans. Allergy accounts for a substantial number of human diseases.

This group of diseases is an important health burden as can be seen from figures compiled by the National Center for Health Statistics (U.S.). Approximately nine percent of all patients seekingmedical care at a physician's office do so for one of the allergic diseases. In their simplest medical form allergic diseases are due to immunological reactions to environmental antigens which result in symptoms on exposure. Allergic diseases have been traditionally classified into four types, based on the nature of the immunological reaction.[1] Type I, due to IgE antibodies is responsible for the symptoms experienced by one out of every ten members of the general public.[2] This mechanism is responsible for the allergy which affects people in the form of allergic rhinitis (hay fever), a condition which is usually secondary to seasonal pollen allergy. Other forms of this type of allergy are bronchial asthma, atopic dermatitis and less commonly gastrointestinal food allergy. Patients with these allergies usually have a family history of similar disorders. The substances in the environment that cause this type of allergy may be either inhaled, ingested, or come into direct contact with the skin.

Inhalants: The most common environmental factors which cause allergy are inhaled and the most common of these are plant pollens, fungal spores, animal danders and air borne particles in the home. Trees, grasses and weeds pollenate each year at predictable times. Spores of fungi

are important environmental allergens and are found outdoors throughout the year except when there is a snow cover on the ground. House dust is the most common indoor allergen and for many dust sensitive patients, the allergen is a tiny mite residing in house dust. The patient's occupation can sometimes be responsible for allergy and an example is baker's asthma. The repeated inhalation of wheat flour by bakers results in hay fever or asthma in about twenty-five percent of bakers.

Ingestants: Allergic symptoms to foods, food additives and drugs can occur through the ingestion of environmental substances and the absorption of those from the intestines.

Contactants: Direct skin contact with a pollen or other allergens can cause hives or some of the other allergic symptoms in a patient who is highly sensitive.

Gell and Coombs defined three other types of allergic mechanisms, all due to immunologic reactions which either destroy cells directly as with certain type of drug reactions, or lead to local tissue inflammation and swelling or lead to contact dermatitis.[1] More recently two further types (Type V and Type VI) of immunological reactions have been described. In these types there are either allergic responses to receptor molecules on cells resulting in, or contributing to, diseases such as diabetes or myasthemia gravis or inappropriate activation of the body's complement system.

Diagnosis: The diagnosis of allergic diseases due to environmental allergens is dependant on three sequential and interrelated steps or procedures. Of these the single most important is the detailed history obtained from the patient in which an association of symptoms with specific environmental agents is attempted. Because of the multitude of environmental agents and often their simultaneous occurence, this history taking is facilitated by a thorough knowledge of the occurence, distribution, periodicity, symptoms, signs, laboratory abnormalities and in the variations in the natural course of responses to environmental antigens.

The second step if required is skin testing for immunologically mediated hypersensitivity. This step may be carried out after the history has suggested the relevant allergens for testing. The skin test is intrepreted shortly after introduction of the antigen into the superficial layers of the skin. The skin reaction is similar to the allergic response that is occuring in the body in response to the allergen, that is the nose in hay fever or the bronchi in asthma.

While skin testing has been the most commonly employed method to attempt to confirm specific sensitivity in patients with atopic disease or anaphylaxis, its intrepretation is fraught with difficulties, particularly, false positive and false negative test results. A laboratory test, the

radioallergosorbent test (RAST) avoids the potential risk or discomfort of skin testing, but while valuable for research purposes, has limited use clinically because it has less applicability, is less sensitive than skin testing, and is more expensive.

The third step in establishing a diagnosis of allergy is through the actual treatment methods, such as avoidance of the allergen. The response to avoidance can be used to confirm clinical suspicions. Again there are pitfalls in the interpretation of the results of treatment because of variations in the natural course of the disease, the placebo effect and other confounding factors.

c) Occupational Medicine and Toxicology:

In addition to the allergens in the general and home environment there has been increasing concern about indoor air quality in the work environment. The number of individuals attributing some ailment to the time they spend in a particular building, usually their place of work, has tripled since the early 1970's. This has led to terms such as "building sickness" and "tight building syndrome".

A harmful effect of the work environment on an individuals' health is well known and includes such diseases as silicosis and asbestosis; two of many examples. The occurance of pollutants in the work environment has led to legislative control and in medical practice to the emergence of specialties for the prevention, diagnosis and treatment of occupational diseases. The changing pattern of industry and labor has moved millions of workers into office buildings, to perform services or process information and has spawned another generation of occupational health concerns. Few work environments would appear safer than the modern office with its sealed windows and carpeted floors filtering out all the harshness of the outside world. However, the building environment can harbour a variety of pollutants which have the potential to adversely affect the health of the individual. Building sickness or tight building syndrome was relatively rare before 1977 but by 1980 it had become a major concern of the National Institute for Occupational Safety and Health, and the Center for Disease Control. Unlike the work related hazards of earlier eras, building sickness has shown no social or geographic preferences, ranging from modest units to skyscrapers. Rarely have investigations of suspect buildings turned up excessive concentrations of any single contaminant. However, sensitive monitoring has often uncovered a number of potentially toxic substances ranging from fiberglass, asbestos and carbon monoxide to phenol, methanol, toluene, xylene and trichloroethane in the same building, though each contaminant may occur in concentrations a hundred or even a thousand times lower than industrial safety standards would permit.[3]

"Building sickness" generally takes one of five forms, four of which can be linked to a specific type of indoor pollution.[3]

The best documented of these is allergic alveolitis, a condition characterized by shortness of breath, cough and flu like symptoms such as headache, malaise, fever and aching muscles. It is an inflammatory condition affecting the terminal bronchial tree and alveoli or the tiny air sacks in the

lungs. Mild allergic alveolitis is commonly called humidifier fever, because the organisms that cause it often dwell in the stagnant water of air conditioners and humidifiers. Outbreaks of this condition are nearly always linked directly to high levels of airborne microorganisms within a building.

Another category of "building sickness" is that of common allergies such as hay fever or bronchial asthma that are aggravated by the prevalence of airborn allergens within a building. These conditions are not due entirely to the situation inside a building as they are caused by fungi, mites, dust or pollens that occur naturally in the environment but may accumulate indoors.

A third type of "building sickness" is infectious diseases that can flourish in a poorly ventilated building. The simplest would be the rapid spread of the common cold or flu epidemics in a shared indoor space. But more important are the respiratory illnesses due to Legionella pneumophilla, which may occur in a pneumonic or non pneumonic form.

A fourth class of building related sickness consists of rashes, itching and eye irritations, and/or throat irritations caused by airborne particles of synthetic materials such as fiberglass insulation.

These four classes of building sickness are all fairly easy to diagnose and eliminate, but together they account for about forty percent of building related health complaints. The majority, fully sixty percent, fall into the category of undiagnosed mucous membrane irritations, such as sneezing, headaches and soreness of the eyes, nose and throat. Many of these are due to the poor quality of indoor air. The National Institute for Occupational Safety and Health in the United States, in investigating 350 complaints up to December 1985, attributed only a small number of these to cigarette smoke, nineteen percent to other contaminants originating inside the building and eleven percent to the entrapment of outside pollutants while fifty percent were attributed to inadequate ventilation and eleven percent to unknown factors.[3]

Thus in the majority of instances investigations of buildings fail to turn up any evidence that specific substances have accumulated in concentrations which would explain these symptoms. It may be that this surge in undiagnosed afflictions reflects a heightened awareness of environmental conditions. Such suspicion of our environment is a good thing to the extent that it makes us more vigilant and less reluctant to question the safety of our working and living conditions. But, to the extent that the sick building syndrome is a expression of our anxieties, it becomes an important social problem . Bardana has stated that "for most of our office workers, fear is probably the greatest occupational hazard of all".[3]

d) Post Infection Syndromes:

Two or three syndromes are associated with severe fatigue and other symptoms in common with those experienced by patients described as suffering from the "total allergy syndrome", "twentieth century disease", and "environmental hypersensitivity". Neuromyasthenia is the name applied to a condition observed in soldiers, health care workers, in other clusters and in epidemics, such as the one that swept through Iceland (hence the term Iceland Syndrome),

and subsequently referred to as epidemic neuromyasthenia.[4-7] More recently such symptoms have been reported as occuring in post viral fatigue and also have been seen with chronic Epstein-Barr virus infection.[8,9]

Patients with the type of neuromyasthenia which occurs in epidemics tend to have headache, aching pains in the extremities, neck and back with paresis in one or more muscle groups. Malaise and fatigability are particularly pronounced and persist long into convalescence. Some patients with the post viral fatigue syndrome show histologic changes in muscles. Scattered muscle fibre necrosis were found in 75% of the biopsies and elevated titres against Coxsackie B viruses were found in 70% of patients.

The recently described syndrome, chronic EB virus infection, has some symptoms similiar to those seen in patients with "neuromyasthenia". Individuals believed to have this syndrome complain primarily of profound almost disabling fatigue as well as myalgia, recurrent mild pharyngitis, painful cervical adenopathy, intermittent fever, depression and difficulty in concentration. Physical examination of patients diagnosed as having chronic EB virus infection is usually unremarkable though if patients are repeatedly examined, low grade fever, pharyingitis and painful adenopathy are generally present, at least at some point in the course of the illness.[10] Some laboratory abnormalities of a non-specific nature are often present and there may be anti EBV antibodies, although these overlap the titres found in normal subjects.

Caution is used in assigning the diagnosis of chronic EB virus infection to a patient because several patients followed for prolonged periods with a working diagnosis of chronic EB virus infection eventually have been recognized as having systemic lupus erythematosus, ankylosing spondylitis and lymphoma. The syndrome resembles multiple sclerosis and epidemic neuromyasthenia in many aspects.[10] Currently it is considered that patients with appropriate signs and symptoms of EB virus infection and with either markedly elevated titres of antibody or individuals with less strikingly elevated titres but whose symptoms date back to an episode of acute infectious mononucleosis, probably have chronic EB virus infection. The large group of individuals who have similar symptoms but who do not meet the above criteria are considered less likely to have chronic EB virus infection.[10]

e) Fibrositis and Fibromyalgia:

This is another ill defined syndrome, appearing predominantly in females whose major symptom is myalgia with several points scattered over the body which trigger the pain.[11] These patients are said to have an abnormal sleep pattern and some respond to low dose tricyclic anti-depressant drugs.

f) Total Allergy Syndrome, Twentieth Century Disease and Environmental Hypersensitivity; Clinical Ecology:

A specific function of this Committee was to advise the Minister whether the condition variously known as environmental hypersensitivity, total allergy syndrome or twentieth century disease exists.

Environmental hypersentivity, total allergy syndrome and/or twentieth century disease are popular terms for a multiplicity of symptoms felt to be due to environmental factors such as food, water, chemicals and pollutants. These terms appear to have their origin from clinical ecology, an approach to medicine that ascribes a wide range of symptoms to exposure to numerous common substances in the environment. Practitioners who subscribe to clinical ecology refer to themselves as "ecologically oriented" and patients are said to be "environmentally ill or hypersensitive or allergic to environmental factors". According to clinical ecologists, patients with environmental sensitivities usually have a multiplicity of symptoms involving many parts of the body. "The chief complaint is minimized or preferably omitted, in view of the characteristic multiplicity of complaints of most ecology patients" (Randolph 1982).[12] These symptoms can range from physical reactions such as running nose, abdominal bloating, headache and fatigue to psychological symptoms such as anxiety, depression and difficulty in concentration. Some of the symptoms and syndromes to which environmental factors have been reported to contribute are shown in Table I as taken from Bell, 1982.[13]

It is suggested that patients said to be hypersensitive or allergic to environmental factors develop an adverse host response after prolonged environmental exposure. Once such "sensitivity" has occurred, the individuals become sensitive to multiple other environmental exposures (foods, chemicals, etc.).

There are very few symptoms that have not been considered to be related to such a presumed etiology and clinical ecologists feel these are "best referred to as polysymptomatic syndromes".[12] Theron Randolph, a founder of the clincal ecology movement, believes that traditional allergy, as described in the earlier portion of this report (Section IIb), is restricted by definition.[12] In his view, each person exists in a dynamic equilibrium with his environment and with an adaptation to the environment. When this adaptation becomes deranged, i.e., maladaption, either acute or chronic illness results. He claims that the primary aim in clinical ecology is the demonstration of etiology, i.e., "the cause and effect relationships between given environmental exposures and specifically susceptable persons".[12]

Clinical ecology is felt to be an "effective alternative to the increasingly expensive drug, hospital and laboratory orientation of medical practice".[12] (The Nova Scotia data in respect to cost is shown later in this report.) Clinical ecologists consider allergic diseases, as presently recognized and as described above (Section IIb), are just one component of the disorders resulting from the diverse human reactions to environmental contaminants in air, water, food, drugs and habitat.

Clinical ecology bases its procedures on two main hypotheses: (1) that the total load of low dose environmental stressors is important in the induction of illness and (2) that changes in the frequency of and intervals between exposures to a specific substance can mask the clinical manifestations of, or alter the degree of sensitivity to, that substance. Clinical ecologists focus on psychiatric, central nervous system and psychophysiologic syndromes which they believe are the result of sensitivities to environmental agents (Bell 1982)[13].

Total load: The first hypothesis in clinical ecology is that the onset of illness depends on the total stress load, including all of the psycho/social, physical, chemical, antigenic, or infective stressors that impinge on the individual. Clinical ecologists suggest that low doses of substances which singly might be benign may interact additively or cumulatively on some common pathways in the body to produce illness. Clinical ecologists believe that illness appears when the total stress loadexceeds some threshold for the patient and that recovery can occur when the total load is reduced below that threshold. Bell states that no direct experimental tests have been done on the validity of the total - load hypothesis and while there are certain epidemiological data consistent with the hypothesis, the retrospective nature of those studies also leave the data open for other interpretations[13].

Adaptation: The second major concept in clinical ecology is that of adaptation. According to clinical ecologists, the greatest response to many stressors is usually evoked by the initial exposure after sensitization has developed. If the stressor is repeated often enough, however, the body adapts by progressively dampening its acute response to each subsequent exposure. Eventually the patient adjusts to the extent that function appears almost normal after recurring exposures to the stressors. A common example given by clinical ecologists is the response to tobacco smoke. A person may cough, choke and feel dizzy with the first cigarette but have minimal acute symptoms with chronic cigarette usage. Meanwhile a chronic illness such as lung cancer may be developing insidously although the marked acute symptoms after each cigarette may be greatly diminished. Similarly they cite as another example, a patient with the potential for rheumatoid arthritis might originally notice acute flares of joint pains and lethargy within hours after eating an occasional hamburger. If the patient begins to eat beef daily, he or she may then develop rheumatoid arthritis after a few months. Chronic joint stiffness and pain as well as joint deformities would then have no obvious relationship in time to a particular meal containing beef. Thus recurrent exposures to non tolerated items may induce adaptation that would mask the acute worsening of symptoms after any given exposure, while still permitting chronic damage.

These low grade symptoms and the adaptation process means that patients and physicians fail to suspect some environmental substances in the etiology of various chronic syndromes. Recently it has been postulated that these chemical and food sensitivities are related to malfunction of the immune system that has been termed immune system dysregulation. This concept has been described as follows:

> Immune system dysregulation can develop over a long period of time and can be triggered by a single serious viral infection, major stress, fungal infection, particularly candida albicans, and accumulative exposure to toxic chemicals, even at low levels found in our everyday

> environment or massive chemical exposure. Immune system dysregulation often remains undiagnosed, however, because many physicians faced with its incredible array of seemingly unrelated symptoms are not familiar with the available diagnostic methods and misdiagnose it as stress, psychosomatic disease or the like. The malfunction commonly originates with the T cells. When the normal complement of T cells are reduced in number or when their ability to function is impaired, they can no longer adequately control B cell production of antibodies. Without this control, the B cells cannot distinguish harmless dust, pollen, animal dander or vital and nutritious foods from toxic chemicals or life threatening bacteria or viruses. The actual healing process from immune system dysregulation i s long, slow, and punctuated by exasperating short term set backs. These set backs are part of the healing process and invariably follow a roller coaster pattern. The frequency, duration and severity of set backs gradually diminish until symptoms are mild and occur only occasionally." (Position paper of the Soc for Clin Ecol 1983-84; cited in [14])

However no consistent immunological abnormalities have been demonstrated in these patients.[15]

Many aspects of clinical ecology are said to relate to toxicology. Clinical ecologists suggest that many substances, such as common foods that are not felt to be toxic ordinarily, are potential triggers of illness. Clinical toxicologists are generally concerned with substances that are more consistently toxic. Clinical ecologists on the other hand state that safe thresholds for exposure to any given environmental agent may not exist for any particular patient and that low doses of substances, expecially in combination with one another as part of the total load, may be harmful to larger segments of the population than many toxicologists recognize.

Clinical ecology has had surprisingly little impact on the practice of medicine and psychiatry. Bell states: "the reasons for this are complex. They include clinical ecologists lack of rigorous documentation, the anecdotal nature of the findings and the interdisciplinary nature of the work. The latter means that clinical ecology lacks a single traditional field which could accomodate it and test its basic concepts" (Bell, 1982[13]).

Clinical titration is the procedure used in clinical ecology to identify sensitivity. The first part of this procedure is similar to the skin test described above (Section IIb) but it is followed by subsequent application of weaker or stronger dilutions of the same antigen to "neutralize" the reaction. This provocation/neutralization test was devised by Carlton H. Lee in 1959 and published in 1961-62.[16]

During his years of investigation Lee observed many bizarre and unusual symptom responses. The provocative - neutralization procedure he developed involves the injection of test doses of "chemicals" or "allergens" to see whether symptoms appear or disappear. During the testing the examiner must evaluate the patient including subtle changes in attitude, behaviour, voice tone and look for signs of urticaria, upper and lower respiratory distress, such as sneezing, nasal stuffiness and wheezing. Unlike the skin testing in allergy and immunology, clinical ecologists do not consider it necessary for there to be a positive local response at the site of the injection in order

to infer that the injected substance is causing an untoward reaction in the patient. Once the symptoms have been provoked, a weaker or stronger dilution is administered in an attempt to relieve the symptoms. The dilution that relieves symptoms is termed the neutralization dilution. Treatment involves long term administration of the neutralizing dilution in a prophylactic manner. The frequency is determined by individual patient variation.

The American Academy of Allergy and Immunology has published position statements concerning these subcutaneous and sublingual provocation neutralization procedures and reported that they are unproven. Newer submissions to the Practice Standards Committee of the Academy have not changed that recommendation.[14]

A further testing procedure used in allergy and immunology and in clinical ecology is elimination of a suspected antigen from the environment and the inference that an improvement in symptoms is due to this withdrawal. In clinical ecology, treatment based on removal of or withdrawal from agents or substances suspected of causing symptoms may lead to substantial environmental and dietary modifications.

III CAUSAL INFERENCES:

In previous sections in this report the Committee has reported on methods used to determine whether the symptoms suffered by a patient are due to a particular agent or chemical and has referred to factors which confuse or confound such interpretations, such as the multiplicity of agents in our environment which make it difficult to ascribe symptoms to any particular one. These confounding effects are powerful and have plagued the medical sciences in trying to establish cause and effect relationships. Because of these considerations and in an attempt to avoid in so far as possible false positive and false negative associations, criteria have been developed over many years to assist in the determination of valid causal relationships. These criteria include the time sequence of variables; the consistency of associations on replication; the strength of the association; the specificity of the association and logic of the explanation (Susser 1973).[17] The best evidence for a causal relationship in modern medical practice is that obtained through randomized clinical trials, particularily those with few false positive or false negative results (Sackett 1986[18]). However for many disorders randomized controlled clinical trials have never been carried out, and much of the information we have on which to base medical decisions have only been simple observations. Moreover an experiment to establish a cause and effect relationship may be very difficult or even impossible at this time.

What rules of evidence ought to apply then when expert Committees meet to generate recommendations for the clinical management of patients? Should only the thoroughly validated results of a randomized clinical trial be admissible to avoid or minimize the application of useless or harmful therapy? Or, in the interest of providing patients with all potential benefits including those

possible from unproved remedies, should the experiences of experienced clinicians form the basis for such recommendations?

That type of evidence which is simply based on observations, which is not based on controlled experiments, and which forms the remembered experience of seasoned clinicians, will tend to overestimate efficacy. It will overestimate efficacy for the following reasons: (Sackett 1986[18])

1. The favorable treatment responses are more likely to be recognized and remembered by clinicians when their patients comply with treatments and keep follow up appointments. However there are already five documented instances in which compliant patients in the placebo groups of randomized trials exhibited far more favorable outcomes (including survival than their non compliant companions). Because high compliance is therefore a marker for better outcomes, even when treatment is useless, our uncontrolled clinical experience often will cause us to conclude the compliant patients must have been receiving efficacious therapy.

2. Unusual pattern of symptoms or signs and extreme laboratory test results, when they are reassessed even a short time later, tend to return towards the more usual normal result. Because of this universal tendency for regression towards the mean, any treatment (regardless of its efficacy), that is initiated in the interim may appear efficacious.

3. Routine clinical practice is never "blind", and both patients and their clinicians know when active treatment is underway. As a result, both the placebo effect (which has shown, for example that angina pectoris can be relieved by the skin incision of a mock internal mammary ligation) and the desire of patients and clinicians for success can cause both parties to overestimate efficacy.

For the preceeding reasons, the "consensus" approach based upon uncontrolled clinical experience risks precipitating the widespread application of treatments that are useless or even harmful. These same treatments are much less likely to be judged efficacious in double blind, randomized trials. Vital decisions may have to be made however on the basis of observational evidence. It is therefore important to have some basis for deciding whether an association derived from an observational study represents a cause and effect relationship. Factors that should enter into this consideration include the strength of the association; the time sequence, its consistency with other knowledge; failure to find other explanations for a phenemona and other criteria such as gradient of risk, consistency in several studies, and specificity.

This discussion should not be misinterpreted as constituting a mandate for discarding those uncontrolled observations by clinicians.What it does mean is that it is important, whenever possible, to base firm recommendations (and especially those involving risk or cost to patients) on the results of rigorously controlled investigations and to be much more circumspect when recommendations rest only on the results of uncontrolled clinical observation.

IV. ADVISORY COMMITTEE ON ENVIRONMENTAL HYPERSENSITIVITY

The Environmental Hypersensitivity Advisory Committee to the Minister of Health held fifteen meetings throughout the summer and fall of 1986. Our study of this subject can be considered under three general headings; a) current theory, and the diagnosis and treatment of patients with environmental hypersensitivity; b) medical aspects of environmental hypersensitivity in Nova Scotia; and c) determining the concerns of individuals who believe they may be suffering from environmental hypersensitivity.

a) Current Concepts in the Theory, and the Diagnosis and Treatment of Environmental Hypersensitivity.

The Committee had available to it a large body of scientific, medical and lay literature, including two reports for the Ministry of Health in the Province of Ontario, for review (The Thomson Report and The Zimmerman Report[19,20]). Some of this literature is reviewed in the previous section of this report (Section II). In addition the Committee invited four experts to visit Nova Scotia and discuss certain aspects of the subject with the Committee. These individuals were Dr B. Zimmerman, Head of the Division of Allergy and Immunology of the Hospital for Sick Children, Toronto; Dr J. Brostoff, Consultant Immunologist, Middlesex Hospital, London, England; Dr J.J. MacLellan, Clinical Ecologist and one of the founders of Clinical Ecology in Canada; and Dr J. Neathercott, Head of the Division of Occupational and Environmental Medicine, University of Toronto and St Michael's Hospital.

Much of the discussion with the invited experts related to modern concepts of environmental sensitivity and their own particular experiences in diagnosing and treating patients with symptoms similar to those observed in individuals in Nova Scotia who suspect they have environmental sensitivity. In addition, four members of the Committee visited the Environmental Care Unit of the Northeast Community Hospital in Dallas, Texas, where Dr W.J.R. Rae is Director. An opportunity was provided to visit patients in the inpatient unit, to review their symptoms and discuss their diagnosis and treatment and to observe and discuss the facilities. During the same trip the private outpatient facilities of W.J. R. Rea and Associates Inc., Dallas were visited, where it was possible to observe testing procedures used to establish the diagnosis of environmental hypersensitivity and to hear presentations from Dr Rea and his associates.

The current literature and the presentations of the experts consulted by the Committee is summarized below.

Allergic symptoms and hypersensitivity reactions are recognized by all practitioners. In addition there are well recognized occupational illnesses and toxic and pharmacological effects of chemicals in our environment, the effects of which are not mediated by immunological

mechanisms. Virtually all practitioners would also agree that there is a group of patients who feel they have environmental sensitivities and who have multiple symptoms as outlined in Table 1. It is also generally agreed that patients who have this grouping of symptoms usually do not have any abnormal physical findings related to these symptoms and ordinarily they have normal laboratory test results.

Some patients with this group of symptoms are believed by clinical ecologists to be suffering from hypersensitivity to a wide variety of environmental substances. The usual method used by clinical ecologists to confirm the diagnosis of environmental hypersensitivity in these patients is a skin or sublingual test or inhalation challenge. The provocation of symptoms by these procedures is interpreted as a positive response regardless of the presence or absence of local reactions to the skin test. If such a "response" occurs, an attempt is then made to remove from the environment "chemicals" or "allergens" or to conduct "desensitization" through injection of those substances, largely identified through the skin testing procedures just described.

There is considerable reservation about the claims of clinical ecologists because of: a) the lack of a scientifically acceptable mechanism or theory to explain why multiple systems are affected with sufficient severity to cause such marked and disabling symptoms in the absence of appropriate physical and laboratory findings reflecting the patients' profound disability and the proposed interference in cellular function, b) the use of testing procedures which have not been scientifically validated, and c) the use of treatment procedures which are often very costly, involve considerable personal and family sacrifice and inconvenience, and for which there is inadequate evidence of reversing or ameliorating disease.[14,15,21] These deficiencies have led to an unwillingness to accept "Total Allergy Syndrome", "Twentieth Century Disease", and "Environmental Hypersensitivity", as a diagnostic entity, specific disease or condition to account for the type of symptoms shown in Table I.[14,15,21]

b) Medical Aspects of Environmental Hypersensitivity in Nova Scotia.

The Committee reviewed the medical problems of patients in Nova Scotia who believe they have environmental hypersensitivity. Two methods were used to carry out this review.

i) Patient Reviews: Eighteen patients were presented to or interviewed by the Committee during the course of this study. The presentations were made by their attending or consulting physician who provided the Committee with relevent and necessary medical documentation. A summary of some of the clinical features of these patients is shown in Table II.

ii) Questionnaire study: A questionnaire was prepared by members of the Committee with advice from Dr. Alex Richman of the Department of Preventive Medicine, Dalhousie University. The questionnaire was distributed by the Directors of the Allergy and Environmental

Hypersensitivity Society to approximately 100 families who were known to the Society. The questionnaire had seven sections as follows:

Demographics - questions 1 to 16
Experience with health professionals - questions 17 to 23
Medical background - questions 24 to 33
Environmental factors - questions 34 to 45
Table regarding symptoms - question 46
Descriptions of attacks - questions 47 to 50
Clinical course - questions 51 to 58

Forty-eight responses from 43 families were received. A summary of the responses by individual question is given in Appendix 1 and summarized in Tables III to XIV. From a review of these responses the following points seem to emerge and to be noteworthy:

1. The listed occupations provides no evidence of the liklihood of industrial exposure to chemicals.

2. A large proportion of the respondents are university graduates.

3. There was a modest number of days lost from work by those who were working compared to the number of physician visits.

4. A large proportion of those who were unemployed attributed their unemployment to their illness.

5. The average age the illness developed was 23.2 years. The average age at present is 38.6 years. (This figure is remarkably constant in several series which have been published).

6. The number of physician visits seems extremely large, if correctly reported.

7. All of the 22 individuals who visited a clinical ecologist felt they received benefit. This may reflect the population responding to the questionnaire as well as the treatment of the ecologists as related to the nature of the illness.

8. The majority of respondents felt they should be referred outside Nova Scotia.

9. A review of previous and current illnesses did not suggest that many respondents had a specific disease that responded poorly to medical therapy. "Asthma" and "respiratory allergies" may be exceptions but it is difficult to be sure of the reliability of these diagnoses.

10. The respondents report a high incidence of affected family members though not the father with one exception.

11. The majority reported they improved due to treatment given but full recovery was rare.

12. The financial impact if reported correctly, is staggering. In contrast to the adults, all of the expenses for children are concentrated in environmental modification and "other expenses". What these "other expenses" represents is not known, perhaps due to some omission in the questionnaire.

13. It was not possible to reconcile the respondent's responses to the question about special exposure to chemicals as being due to their occupation or hobbies. The reference to chemistry chemicals is intrepreted as chemicals in teaching chemistry laboratories involving teachers or students. Many of the other chemicals may be those encountered in every day life.

14. A very high proportion of respondents live in houses rather than apartments. Virtually all of those who moved state that they improved.

15. A large porportion experience their symptoms in attacks. Almost all attacks occur in certain locations. However the locations are very diverse and the responses reflect perceptions of exposure to etiological agents rather than particular locations.

16. Clustering of attacks at certain times reflect differences in seasons rather than time of day, with one exception.

17. Most respondents are still having attacks in 1986.

c) Patient Concerns & Recommendations: Allergy and Environmental Hypersensitivity Society.

To determine some of the concerns of individuals who believe they are suffering from environmental hypersensitivity eight patients were interviewed, one patient was interviewed at home and the environmental modifications made to the home were observed, and a number of appropriate questions were included in the questionnaire. In addition the Committee met with some of the Directors of the Allergy and Environmental Sensitivity Society of Nova Scotia. The reponses to the questionnaire can be found in Appendix 1 and the recommendations of the Allergy and Environmental Sensitivity Society are shown in Table XV.

V. CONCLUSIONS AND RECOMMENDATIONS OF THE ADVISORY COMMITTEE ON ENVIRONMENTAL HYPERSENSITIVITY

Increasingly Nova Scotians have been concerned about the state of their environment. This concern arises because of their belief that natural and man made chemicals and substances in the environment can induce allergic, toxic and pharmacologically harmful effects on their life. It is also well known that the number of chemicals added to the environment continues to increase and that some individuals are more sensitive to certain components or substances in the environment than are others, as we have discussed in Section II of this report.

Although there is a very large number of specific chemicals and injurious agents, the body has a limited number of ways in which it can respond to these. Since similiar symptoms occur in response to a variety of diseases or harmful agents it is important that a patient's initial assessment be general or "holistic" to determine the possible causes of these. There are for example several causes of headache, of tiredness, of weakness, and of depression.

Following our review of the clinical information provided to us it was the unanimous opinion of this Committee that the patients whose clinical records were presented to us, or whom we interviewed, had significant symptoms, were unwell and that they will require ongoing

assessment and care. It most instances the specific diagnoses was unclear. Therefore the Committee in formulating its recommendations for the Minister of Health had two objectives:
a) to make statements both on the theory of clinical oncologists which attempts to explain the symptoms experienced by these patients and the procedures used to test and treat them; and b) to ensure there will be appropriate ongoing medical services available to these patients, and others who may be similiarly afflicted, services which will sometimes be of a multidisciplinary nature, including referral to consultants within or outside the Province if this is judged to be necessary. The Committee will also recommend a mechanism to enable this multidisciplinary assessment to occur.

A) COMMENT ON RELATED ISSUES

Before considering a response to the questions directed to us however, the Committee wishes to comment on a few related issues. These comments are intended to provide a further background to our specific recommendations.

1. What is the relationship between "allergy" and "environmental hypersensitivity"?

As outlined previously, allergic diseases primarily include those conditions associated with immediate hypersensitivity such as allergic rhinitis and extrinsic bronchial asthma but would also include conditions associated with other immune reactions such as contact dermatitis and certain drug reactions. The symptoms associated with "environmental sensitivity" have not been shown to be produced by these immunological mechanisms and indeed the principles of total load and adaptation, as enunciated by clinical ecologists imply a separate mechanism of action. We would therefore consider "environmental sensitivity" in this context to be distinct from "classical allergy."

2. What is the relationship between environmental "toxicity" and "sensitivity"?

Most substances foreign to the human body and indeed even constituents of the human body are toxic or capable of producing disease if present in a sufficiently high concentration. Each substance produces characteristic pathology and the effect is dose dependent in that the majority of the population become affected at a definable concentration. The concept of "sensitivity" as proposed by clinical ecologists is quite different in that a subgroup of individuals are affected by concentrations of foreign substances which are well tolerated by the majority. Furthermore, in that subgroup of individuals specific substances did not produce characteristic symptoms but rather were associated with different symptoms in different individuals. We therefore consider that "environmental sensitivity" is a concept that is separate from "toxicity".

3. Is there a mechanism which might explain the production of such diverse symptoms as a result of exposure to foreign substances?

In seeking a mechanism to explain diversity of the symptoms experienced by patients thought to have "environmental hypersensitivity," an appropriate analogy might be to the allergic mechanism alluded to previously (Section ii b). However, while the immunological reactions involved in these allergic diseases can be demonstrated with great precision under controlled

conditions both in the clinical evaluation of patients and in the laboratory, these immunological reactions have not been shown to be responsible for the symptoms of patients thought to have "environmental sensitivity." Furthermore there are several reasons for believing that this would be unlikely. Thus many of the substances implicated in environmental sensitivity are poorly immunogenic. Whereas in classical allergic reactions each immunologically mediated effect is characterized by well defined "latent periods" between exposure and the onset of symptoms, this interval is quite variable in patients said to have environmental sensitivities. Finally immunologically mediated reactions produce characteristic symptoms and pathology depending on the mechanism (pathogenesis), unlike the diverse complaints of patients with "environmental sensitivity."

Clinical ecologists have proposed the "total load - adaption" concept as an explanation. This is based on adaptation to stress as proposed by Hans Selye and in that context has a discernable basis in science, but we have not seen any evidence that patients with "environmental sensitivities" differ from others in this respect. Furthermore we have not been able to identify a link which would explain how adaptation to environmental substances produces the symptoms of these patients. We therefore consider that this concept of environmental sensitivity remains a hypothesis and as yet does not provide an explanation for the mechanism (pathogenesis) of the proposed condition. We recognize that this does not negate the possibility that the symptons are caused by exposure to substances in the environment but this association would need to rest on evidence that is subject to verification.

4. Is there a causal relationship between exposure to foreign substances and the symptoms manifested by these patients?

This question is central to our inquiry. The diagnosis of environmental sensitivity depends on establishing such a causal relationship using the following methods.

(a) Medical history The patient is asked to recall details about the circumstances when symptoms occur. Inferences are then made about causative or contributory factors based on the likelihood of exposure to these factors under these circumstances, knowledge of the latent period between exposure and symptoms, knowledge of the type of symptoms usually produced by different environmental agents and the consistency of these associations. This information is indispensable in the investigation of allergic problems and causal inferences can be drawn with considerable confidence in the case of seasonal symptoms due to pollen allergy or immediate sensitivities to animal or certain food allergens. The history is not as easy to interpret when the allergen is more ubiquitous as in dust sensitivities. A recognized problem in obtaining an accurate history is a tendency for patients to assume that there is a consistent relationship between exposure to a substance and the appearance of symptoms if they are led to believe they are allergic on the basis of other evidence. The problems in interpreting the history are compounded in the case of "environmental sensitivity" in that a large number of environmental agents have been implicated in

its causation, many of which are encountered frequently or continuously in everyday life, virtually any symptom has been attributed to such exposure and the latent period is extremely variable. We are therefore reluctant to draw causal inferences from personal observations alone.

(b) Tests for environmental sensitivity. The most commonly used tests are skin tests or sub-lingual tests as outlined previously. When many substances are tested, testing often proceeds for a prolonged period of time with the results depending on aggravation or amelioration of symptoms. This is a subjective end point and we are concerned about the possibility of introspection, of suggestion, or of coincidence influencing the intensity of symptom during this period. The reliability of these tests has not been validated and we do not accept nor recommend them as a means to make diagnoses.

(c) Response to treatment. Virtually all of the respondents we surveyed felt they improved as a result of treatment, although most were still symptomatic. While this is a selected population, it seems clear that certain patients are less symptomatic when treated by clinical ecologists. Such symptomatic improvement is put forward as evidence that the symptoms resulted from exposure to foreign substances. Treatment is often multifactorial, involving injections, dietary manipulation, changes in lifestyle, environmental changes, counselling, and reassurance about the diagnosis. In view of these multiple variables and the subjective nature of the response, we consider that it is hazardous to draw the conclusion that the symptoms were due to exposure. Indeed, other equally plausable explanations could be offered. Uncertainties of this kind are usually resolved by rigourously controlled therapeutic trials. These have not been conducted in the case of "environmental sensitivity." We recognize that improvement may occur, (although complete relief of symptoms is unusual), but believe that it is premature to conclude that "sensitivity" is the basis for the complaints of these patients.

5. Are there other explanations for the symptoms of patients who are felt to have environmental sensitivity?

The symptoms commonly described such as fatigue, headache, muscle aches etc., are extremely non-specific in that they can occur individually in a large number of pathological or physiological states. It is therefore important to recognize the possibility that some or all of the symptoms in a given patient may be due to unrecognized underlying disease. Many of these patients have had extensive investigations without evidence of demonstrable pathology, making other diseases less likely. However, some diseases produce subtle findings and it is quite possible, for example, that chronic viral infection or a "post viral state" could mimic the clinical presentation of "environmental sensitivity." The similarity of these symptoms to those of emotional stress has also been noted and several studies have emphasized the importance of psychological factors. At the present time we recognize that there are several possible explanations for the symptoms of these patients and they may well be heterogeneous in this regard.

6. Regardless of causation, should environmental manipulation be encouraged if it results in symptomatic improvement?

This is a philosophical, ethical, sociological and economic question as well as a medical one. There seems little doubt that many of these patients are extremely anxious and frustrated when chronic disabling symptoms are not adequately explained after extensive investigation. Reassurance that a definite external cause has been found would understandably provide immense relief in these circumstances even if the diagnosis of "sensitivity" was based on uncertain evidence. However, we perceive serious consequences unless the diagnosis is based on solid evidence. The perception that ordinary environmental conditions are hazardous can lead to marked changes in lifestyle with termination of employment, disruption of social activities, and ruinous expense if attempts are made to change the environment by moving or renovations. Furthermore, since virtually every symptom has been attributed to "environmental sensitivity", the practice of accepting this diagnosis on circumstantial evidence, with or without professional advice, will almost certainly lead many other individuals with minor or unexplained symptoms to believe they are suffering from environmental sensitivity. We recognize the desirability of advising patients with certain conditions such as chronic rhinitis or bronchial asthma to improve the quality of indoor air by such measures as adequate humidification and ventilation, dust control and avoidance of volatile compounds inconcentrations which have been shown to irritate mucous membranes. However this type of advice should be tailored to individual circumstances and should not extend beyond diagnostic entities which can be substantiated by accepted criteria. Those who advocate such changes should demonstrate, (using the scientific method) that such changes are benefical. We would conclude that unless a causal relationship has been established by other means, it is proper to resist the temptation to use the perception of environmental sensitivity as a therapeutic tool.

B) COMMITTEE'S RESPONSE TO SPECIFIC QUESTIONS IN ITS TERMS OF REFERENCE

Turning to our specific function the Committee has the following comments in response to the questions directed to it.

I. Is there an identifiable condition known as Environmental Hypersensitivity "Twentieth Century Disease" or "Total Allergy Syndrome"?

The Committee is of the opinion that there is no scientific evidence to support the existence of an identifiable condition known as "twentieth century disease" or "total allergy syndrome" or "environmental hypersensitivity" considered in a similar context. The Committee again wishes to emphasize that it recognizes the important influence of noxious elements in the environment and that there are clearly recognized diseases and disorders which are caused by or aggravated by components of, or elements in, the environment. The Committee also recognizes that there is controversy about the existence of this variably described condition. However, the condition

variously described as total allergy syndrome, twentieth century disease or environmental hypersensitivity, in the context presented to and reviewed by us, does not have an acceptable scientific basis. In our opinion, the intradermal and sublingual tests used to identify putative agents responsible for this condition also do not have a scientific basis, and we consider them inadequate tests on which to base diagnosis or treatment.

We have arrived at this conclusion in part through extensive review of the medical scientific literature, through a study of the writings and publications of clinical ecologists, through interviews with clinical ecologists, immunologists and allergists and experts in occupational medicine and a visit to one of the best known integrated hospital-private practice arrangements, through study of patient records in Nova Scotia and interviews with some patients, and through a questionnaire survey of patients in this Province who believe they have environmental hypersensitivity.

The Committee feels that the problems of the patients who were the subject of our review ought not to be left at this level however, that is essentially undiagnosed. We have previously indicated we believe they are not well and that many seem to have multiple symptoms related to a number of body organs and systems, and are thus "multidisciplinary problems". In the following sections of this report, and in answering the additional questions in our terms of reference, we will attempt to provide a mechanism, which, over a two or three year period, could provide a process which would lead to a more accurate diagnosis, for some patients.

2. Are any additional diagnostic or therapeutic services required in Nova Scotia to help patients and their physicians who believe they may be suffering from this condition?

Although the Committee believes there is no scientific evidence for the existence of the condition variously known as "total allergy syndrome" etc. and believes the tests used to diagnose or confirm the diagnosis are inadequate, the fact remains that there are patients who believe they may be suffering from this condition. To determine, the medical needs of these patients in a precise manner, the Committee believes that additional services will be required over a two or three year period.

The patients we have reviewed in detail in Committee sessions and who have completed the questionnaire are undoubtedly unwell and present very complicated, long standing difficult diagnostic and treatment problems for their physicians. We know of several patients who did not complete questionnaires and therefore the number of patients with symptoms similiar to those we have investigated undoubtedly is greater than the 48 to 50 on whom we have information. For some of those who present themselves for care, a multidisciplinary effort may be necessary to try to make the accurate diagnoses that are necessary before appropriate treatment stategies can be developed. Sometimes no accurate diagnosis may be found to account for the symptoms and we expect some may not accept the conclusions of an assessment. While many patients reported some degree of improvement in their symptoms, almost all have continued to have problems for long

periods of time. We therefore anticipate that an important requirement is an ongoing commitment to continued evaluation and care, for a reasonable period of time, after the initial diagnostic procedures have been completed.

The Committee recommends that the Minister of Health, in consultation with the Medical Society of Nova Scotia, cause to be established an appropriate multidisciplinary team of clinicians for the initial assessment, diagnostic evaluation and follow up of patients who believe they have total allergy syndrome, twentieth century disease or environmental hypersensitivity. Further details are provided under (3) and (4) below.

Such a mechanism does not now exist. Currently family physicians who have patients with multiple problems, or multiple symptoms such as the patients who are of concern to us, must not only rely on multiple consultations for complex patient problems, but attempt to integrate all the information alone. In virtually all circumstances such a mechanism is entirely satisfactory because of the expertise of family physicians and the level of consultative support available to them. However we believe that system is "laboring" in trying to meet the needs and assist the patients of concern to us. There are several reasons for this but primarily this is due to the absence of a multidisciplinary environment where a team of health professionals, with appropriate allied health professional support staff, can carry out and discuss the comprehensive assessments necessary for these patients.

We have no illusions that this proposal will be a satisfactory one for all, nor that it will entirely resolve the existing problem. Nevertheless we believe it is the only practical and realistic step to be initiated at this time. We believe the experience gained by the multidisciplinary team will provide the foundation for subsequent recommendations to the Minister of Health and the Medical Society, provided the multidisciplinary team gains sufficient acceptance initially to initiate the assessments, and subsequently not only satisfies referring clinicians but achievies scientific credibility for its assessments from knowledgeable peers.

The time required to coordinate this interdisciplinary review, leads the Committee to recommend that a part time assistant be appointed to help the team coordinate it's activities and data compilation. When appointed the team would define this assistant's duties, which are expected to include at least scheduling, recording of data and administration of questionnaires.

With respect to other diagnostic and therapeutic services the Committee believes that most modern testing methods for allergy and hypersensitivity are now available in this Province as required, based on the type of detailed history essential to the ordering and interpretations of these investigations. However the Committee considers it would be beneficial if there were available facilities for more extensive testing for adverse reactions to foods, such as through the adminstration of foods in capsules so that blind challenges can be accomplished. It is the Committee's intent to leave the detailed recommendations necessary for this procedure with the multidisciplinary team.

In the absence of convincing evidence that the symptoms manifested by these patients are caused by airborne contaminants, the Committee recommends that public funds should not be used in an attempt to reduce the type of exposure encountered in everyday life, at work or at home.

The Committee recognizes the waiting list for patients who are referred to consultant pediatric and adult immunologist/allergists is in the order of three months for elective requests though urgent needs are promptly met. Perhaps additional specialists are required, as for example allergists with a special interest in adverse reactions to food, to complement current specialists interests in the Province. At this time we do not have sufficient information on the medical backround of most of the patients who have that disabling group of symptoms that led to their consideration by this Committee, nor whether the availability of additional medical specialists would affect their diagnosis and management. As these patients are reviewed, through the mechanism we described, the additional specialists, allied health professionals or laboratory support needed will be better clarified and identified and we would prefer to leave the matter of additional specialists unsettled at this time.

It has been suggested to the Committee that a clinical ecologist would be a useful addition to the specialist services of the Province. Given the absence of accepted training and certification programs for this type of practice by the two regulating bodies in this country, the absence of an acceptable scientific base for practitoners who profess this theory, and the lack of acceptable testing procedures and treatment programs, the Committee cannot support such a recommendation at this time. Nevertheless, were it possible to find an adequately trained individual with an interest in clinical ecology/allergy who avoided both the propensity to make scientifically unwarranted inferences and to develop treatment programs based on these, that individual might be helpful in an investigation of some of the patients in the Province, particularly in the study of potential food sensitivities.

Elsewhere in this report, the Committee commented on the diagnostic tests and therapies used in clinical ecology and expressed its lack of confidence in them. We do not recommend that these tests and therapies be insured health services.

3. Is there a medical necessity to refer these patients to a center outside Nova Scotia or Canada for diagnosis/or treatment.

4. If so, what should be the appropriate procedures by which the cases of patients who believe themselves to be suffering from environmental hypersensitivity should be reviewed. In the event that a request to approve an out-of-country referral is received by the Department of Health.

When it is determined that the facilities or personnel necessary for the care of patients for any condition or disease is not available, current policy is that the Province will pay for the required services elsewhere. Assessment of such needs are made on an individual basis. The Committee recommends that this procedure be continued for the patients who have symptoms in the context which we have addressed. However, when an attending physician believes that facilities or

personnel required for a patient problem of the type we have considered are not available in the Province, that patient's problems should be assessed by the multidisciplinary team described above, before public funds are granted for out-of-province diagnosis or treatment.

To carry out the assessment of patients with this symptom complex, the Committee recommends the multidisciplinary team should have representation from the medical disciplines of family medicine, pediatrics, immunology/allergy, general medicine and psychiatry. The members should initially be appointed for a two or three year period, so that a complete review of this method of assessment can be carried out near the conclusion of that period. A decision then can be made as to whether this method of assessment and review ought to be continued.

The clinician team would also review all requests from an attending physician for possible funding for out-of-country diagnosis/treatment of his/her patient, and advise on further consultant(s), within or outside Nova Scotia, who should review the patient's problems. The clinician team could also recommend that outside consultants come to the Province at specific periods to see patients.

The team would receive copies of all medical reports of patients referred to it and by it for assessment so as to be able to evaluate the results of its efforts. The team should also be charged with the responsibility of keeping the Minister informed of any significant developments which might necessitate changes in Government policy respecting patients with the symptoms with which we have been concerned.

We believe the team should encourage educational programs for physicians, in respect to the kinds of problems we have reviewed, through Dalhousie's Division of Continuing Medical Education, when the team has accumulated sufficient information.

Our deliberation over the past several months led us to conclude that the patients who prompted the creation of this Committee are unwell. We have also concluded that there is no scientific evidence that the techniques currently used by clinical ecologists are effective. A number of other Committees across North America have had similar deliberations and reached similar conclusions. It would seem if any real advances in the treatment of these patients is to be made it will only come from careful multidisciplinary clinical evaluation and well designed and executed research protocols. In the first instance descriptive studies will be necessary with the attacks witnessed at first hand under appropriate physiological monitoring. There is an adequate patient population in Nova Scotia to allow this to be done. Future recommendations of the multidisciplinary team that we recommend be set up can then be based on these observations. There are several appropriate ways of designing such studies to control for the many variables which can affect such investigations.

We therefore recommend that the multidisciplinary team, in addition to carrying out comprehensive clinical evaluations, design and carry out such studies after the proposed studies have undergone appropriate scientific and ethical peer review and receive the full informed consent of the concerned patient.

VI. SUMMARY:

The Advisory Committee to the Nova Scotia Minister of Health on Environmental Hypersensitivity was formed in response to a number of requests for out of province referral for this condition. The Committee reviewed a large number of published reports on this subject and interviewed several consultants from outside the province with expertise in this and related medical subjects. We also interviewed representatives from the Nova Scotia Allergy and Environmental Hypersensitivity Society as well as family physicians concerned with the problem, some patients and some members of the Committee visited a patient's home. We reviewed the medical records of certain patients and designed and analyzed the responses to a questionnaire which was distributed to members by the Society. In addition four members of the Committee visited an Environmental Care Unit in Dallas, Texas.

Environmental sensitivity in the context under review is a concept promoted by clinical ecologists whereby it is believed that a large variety of symptoms are produced by the particular susceptibility of certain individuals to many substances normally encountered in the environment. It is distinct from classical allergy in the diversity of the symptomatology, lack of pathological changes and absence of defined immunological effector mechanisms. It is also distinct from toxicology in the degree of individual susceptibility and the variability in the effects produced by a given agent.

The conclusion by clinical ecologists that patients suffer from environmental sensitivity rests on the association between the development of symptoms and exposure to environmental factors in the patient's experience, and on skin and sublingual tests as practiced by the ecologists, and response to treatment.

These diagnostic criteria have not been generally accepted because of the difficulty in correlating multiple symptoms with many different environmental factors some of which are ubiquitous, lack of validation of the tests, and absence of therapeutic trials in which protection from the appropriate environmental factors was the only variable. Although the patients we surveyed felt better by seeing clinical ecologists, we could find no evidence that an objectively defined pathological process was reversed by these treatments.

The Committee is therefore of the opinion that environmental hypersensitivity in the context presented is not an acceptable or valid diagnostic entity.

We are of the opinion that some of these patients would be helped by additional services within the province. We therefore propose that a multidisciplinary clinician team be formed, representing clinical specialities in the disciplines in which patients have symptoms, to help in the assessment of such patients and the establishment of appropriate diagnoses. The team would have the option of recommending to the Minister of Health, the help of out of province consultants.

Table 1 - Reported Symptoms and Syndromes*

1. Skin: Itching, burning, flushing, warmth, coldness, tingling, sweating behind neck, etc. Hives, blisters, blotches, red spots, pimples.

2. Ear, Nose, Throat: Nasal congestion, sneezing, nasal itch, runny nose post nasal drip. Sore, dry or tickling throat, clearing throat, itchin palate, hoarseness, hacking cough. Fullness, ringing or poping of ears, ear ache, intermittent deafness, dizziness, imbalance.

3. Eye: Blurring of vision, pain in eyes, watery eyes, crossing of eyes, glare hurts eyes; eyelids twitching, itchy, dooping, or swollen; redness and swelling of inner angle of lower lid.

4. Respiratory: Shortness of breath, wheezing, cough, mucous formation in bronchial tubes.

5. Cardiovascular: Pounding heart, increased pulse rate, skipped beats, flushing, pallor, warm, cold, tingling, redness or blueness of hands, faintness, precordial pain.

6. Gastrointestinal: Dryness of mouth, increased salivation, canker sores, stinging tongue, toothache, burping, retasteing, heartburn, indigestion, nausea, vomiting, difficulty in swallowing, rumbling in abdomen, abdominal pain, cramps, diarrhea, itching or burning of rectum.

7. Gentourinary: Frequent, urgent or painful urination; inability to control bladder; vaginal itching or discharge.

8. Muscular: Fatigue, generalized muscle weakness, muscle and joint pain, stiffness, soreness, chest pain, backache, neck muscle spasm, generalized spasicity.

9. Nervous system: Headache, migraine, compulsively sleepy, drowsy, groggy, slow, sluggish, dull, depressed, serious, crying; tense, anxious, stimulated, overactive, restless, jittery, convulsive, head feels full or enlarged, floating, silly, giggling, laughing, inebriated, unable to concentrate, feeling of separateness or apartness from others, amnesia for words or numbers or names, stammering or stuttering speech.

*From Bell 1982[5]

TABLE II: Clinical Features of 18 Patients Presented to or Interviewed by the Advisory Committee

Adults	Children	Males	Females	Preexisting Problems	Commonest Major Symptoms
15	3	4	14	allergy 3 infections 3	weakness, fatigue, lack of concentration and mental confusion, headache, muscle aches, pains and spasms, bloating and swelling, diarrhea and abdominal pain, paresthesias i.e. numbness or pins and needles sensation

TABLE III: Frequency of Major Symptoms Respondents To Questionnaire Associate with Environmental Hypersensitivy (Nova Scotia)

Symptom	Number Reporting Symptom
Fatigue	24
Headaches	18
Upper Respiratory Tract Symptoms (sinus trouble, sneezing, sore throat, etc.)	11
Abdominal Symptoms	9
Chest Pain	8
Depression, nervousness, restlessness, panic feeling, etc.	7
Mental confusion or problems in concentration	6
Asthma, wheezing	4
Weakness	4

TABLE IV: Major Symptoms Reported by Questionnaire Respondents in Nova Scotia as being due to Hypersensitivity

General:	Fatigue and tiredness, weakness, coldness, swelling in hands and feet.
Nervous System:	Headaches, depression, inability to concentrate, reduced alertness, poor memory, confusion, stupor, dizziness panic feeling, tingling, light headed, numbness, fragile emotions, tension, irritability, short tempered, mood changes, moody, nervous upset, "toxic brain".
Skin:	Welts, burning and flushing, red cheeks, eczema.
Ear, Nose & Throat:	Dry mouth, burning lips and mouth, canker sores, mouth blisters sinus infection, congestion and pain; stuffed and runny nose, pain in throat, itchy throat, sneezing, suppression of voice, hoarseness, laryingitis, itchy ears and ringing in ears.
Eyes:	Blurred vision, visual disturbances, itchy eyes, irritated eyes.
Respiratory:	Shortness of breath, difficulty breathing, choking, wheezing, asthma, cough, pain in chest.
Cardiovascular:	Palpitations, chest pain, tightness in chest.
Gastrointestinal:	Nausea, gastric upset, cramps and pain in abdomen, digestive and bowel problems, esophageal, spasm, constipation, diarrhoea, gas, bloating.
Gentourinary:	Recurrent vaginitis.
Musculoskeletal:	Muscle tightness, aches, pains, spasms, arthritis, joint stiffness, joint pain.

TABLE V: RECOMMENDATIONS FROM THE ALLERGY AND ENVIRONMENTAL HYPERSENSITIVITY SOCIETY (NOVA SCOTIA)

- clinical ecologist

- psychiatrist or psychologist familiar with cerebral reactions to help patients deal with these reactions and the effects of chronic illness

- antigen program

- antigens without preservatives

- tax considerations for:
  - necessary renovations
  - home relocation
  - less contaminated food and water
  - cleaning services
  - sundries such as oxygen, air clearners/filters, water filters, vacuum systems etc

- support systems such as:
  - homemakers
  - nursing care

- a temporary environmentally safe place for patients requiring major changes, e.g. Sunnyhill

- hospital wing to provide:
  - testing and treatment
  - a safe (environmentally clean and with aware staff) place for treatment of other medical problems.

- education to aid doctors in recognizing this illness, which would result in prompt referrals and fewer unnecessary treatments which can be damaging

- education for patients to assist in their own recovery program

- tests, e.g. blood samples that can detect the presence of chemicals etc. in the blood

- greater emphasis placed on decreasing environmental dangers such as: dry cleaning solution, pesticides, herbicides, chemicals fertilizers, chemical wastes, etc.

TABLE VI **DEMOGRAPHIC DATE**

RESPONDENTS:		48	
SEX:	Males	14	
	Females	34	
AGE:	Mean	38.6	
	Range	7-63	
MARITAL STATUS:	Married	29	
	Single	11	
	Separated	4	
	Widow (er)	2	
	Divorced	2	
OCCUPATION:	Homemaker	15	
	Teacher	6	
	Student	6	
	Other	14	
	Unspecified	7	
EDUCATION:	Grade School	9	
	High School	12	
	University	22	
	Post Graduat	3	
EMPLOYMENT:	Employed:	Yes = 14:	Days lost in the last year: Avg: 9.3 days Range = 1-6- days
			Changed job due to illness Yes = 9 No = 13
		No = 25	Unemployed due to illness Yes = 22 No = 5

TABLE VII: MEDICAL BACKGROUND

Number of physician visits over 3 years:	Adult:	Average =	47.1
		Range =	1-200
	Child:	Average =	10.9
		Average =	1-50
Number of physicians seen:	Adult:	Average =	7.6
		Range =	1-50
	Child:	Average =	3.3
		Range =	1-10

Visited the following in the last year.

	YES	NO	HELPED MOST
ACUPUNCTURIST	7	41	1
CLINICAL ECOLOGIST	22	26	22
CHIROPRACTOR	5	43	0
NUTRITIONIST	17	31	5
NATUROPATH	4	44	2
HOMEOPATH	14	34	10
TRADITIONAL ALLERGIST	25	23	6
PSYCHIATRIST	9	39	1

Visits outside Nova Scotia: Yes = 19 No = 23
Visits outside Canada Yes = 4
Necessity for referral outside Nova Scotia: Yes = 36 No = 7

PAST DISEASES: RESPONDENTS: 47

Infectious disease of childhood	38
Tonsillitis	12
Allergies	9
Asthma	10
Rhinitis/Sinusitis	4
Pneumonia	9
Bronchitis	5
Infectious mononucleosis	7
Migraine	5
Urinary tract infection	4
Appendicitis	6
Arthritis	3
Hypothyroidism	3
Eczema	3
Hives	2
Miscellaneous	19

MEDICATION USED IN PAST:

Bronchodilators	15	Penicillin	7	Other	40
Antihistamines	10	Cortisone	5		
Allergic medication	7	Intal	4		
Vitamins	7	Antibiotics	4		

TABLE VIII: CURRENT MEDICAL CONDITION

Believed to have environmental sensitivities: Yes = 47 No = 0

CURRENT DISEASES:	PRESENT	BELIEVED TO BE CAUSED BY ENVIRONMENTAL HYPERSENSITIVITY
Allergies	13	10
Asthma	8	13
Candidiasis	6	1
Arthritis	5	1
Environmental Problems	5	
Bowel disease	4	2
Headache	4	13
Ear disease	4	
Hypoglycemia	4	3
Migraine	3	7
Diarrhea	3	6
Fatigue	2	4
Sinusitis	1	5
Sore throat	1	5
Other	44	72

CURRENT MEDICATION:

Bronchodilators	12
Antihistamines	8
Vitamins	7
Analgesics	7
Antihypertensive	5
Tranquilizers	5
Others	22

Other family members with environmental sensitivity: Yes = 29
No = 14

Relationship of affected family members:	
Father	1
Mother	11
Children	18
Female Spouse	3
Male Spouse	1
Sister	3
Brother	4

Improvement of symptoms by involvement with support group: Yes = 28
No = 11

TABLE IX **ENVIRONMENT**

Exposure to animals:	Yes = 32	Dog = 17	Rabbit = 1
	No = 15	Cat = 12	Chicken = 1
		Bird = 1	

Special exposure to chemicals due to occupation or hobbies:

None = 9
Dust = 6
Paint = 5
Chlorine = 4
Aerosol spray = 3
Chemistry chemicals = 3
Newsprint = 3
Fuel oil = 3
Formaldehyde = 2
Glue = 2
Insecticides = 2
Molds = 2
Propane = 2
Perfume = 2
Petrochemicals = 2
Others = 26

Accomodation:	House = 46 Apartment = 2
Building Age:	Average = 23.8 years Range = 5 months - 100 years
Heating:	Electric = 15 Hot Air = 10 Oil = 9 Hot water = 9 Wood = 6
Humidifier:	Yes = 19 No = 29
Air Conditioner:	Yes = 11 No = 36
Modification of living environment:	Yes = 45 No = 2
Moved because of illness:	Yes = 17 No = 30
Helped by moving:	Yes = 18 No = 1
Modified diet:	Yes = 46 No = 2

TABLE X **CLINICAL COURSE**

Age when illness developed:	Adults:	Average = 23.2
	Children:	From Birth = 5
		Age 4-5 = 2
Health prior to onset:	Good = 32	
	Poor = 9	
Onset associated with infection:	Yes = 12	
	No = 23	
	Unsure = 8	
Symptoms improved:	Yes - 37	
	No = 9	
Degree of Improvement:	Complete = 1	
	Incomplete = 37	
Has improvement been due to treatment:	Yes = 34	
	No = 4	

TABLE XI :

RELATIONSHIP OF COMMONLY ENCOUNTERED SYMPTOMS TO CLINICAL COURSE

		HEADACHE	FATIGUE	UPPER RESPIRATORY SYMPTOM
SEVERITY:	(a) Mild	3	0	1
	(b) Intermediate	4	2	8
	(c) Severe	5	14	4
PATTERN:	(a) Continuous	2	6	5
	(b) Intermittent	7	3	5
	(c) Continuous with episodes of increased severity	2	7	4
ENVIRONMENTAL FACTORS:	(a) Foods	4	8	6
	(b) Airborne Substances	11	13	13
REASONS FOR IMPLICATING ENVIRONMENTAL FACTORS:	(a) Personal Observation	19	14	14
	(b) Ecology History	7	9	4
	(c) Ecology Tests	7	8	5
	(d) Medical History	8	6	7
	(e) Medical Tests	3	2	3
	(f) Response to Treatment	8	7	10
TREATMENT:	(a) Avoidance	10	13	13
	(b) Diet	4	11	8
	(c) Injections	2	8	6
RESPONSE TO TREATMENT:	(a) Excellent	3	6	4
	(b) Good	4	2	4
	(c) Fair	2	4	4
	(d) Poor	1	1	0

TABLE XII DESCRIPTION OF ATTACKS

Symptoms occurring in attack	Yes = 41	
	No = 6	
Attacks occurring consistently in a certain place	Yes = 39	
	No = 2	
Place identified:	Shopping areas	22
	Smoke	14
	Moldy/Musty are	10
	Traffic	8
	Buildings	7
	Perfume	6
	New Buildings	5
	Chemical areas	5
	Fumes	5
	Paint	4
	Other	34
Attacks occurring consistently at a certain time:	Yes = 18	
	No = 9	
Time identified:	Summer = 3	
	Fall = 3	
	Spring = 3	
	Winter = 1	
	Other = 2	
Date of last attack:	1986:31	
	1985:1	

TABLE XIII **DESCRIPTION OF ATTACKS**

DATES

	LAST ATTACK	2ND LAST ATTACK	3RD LAST ATTACK
Oct-86	1	1	1
Sep-86	3	1	1
Aug-86	9	5	4
Jul-86	13	9	2
Jun-86		1	5
May-86	1	4	1
Apr-86		1	1
Mar-86	3	3	1
Feb-86		1	1
1985	2	2	3
1986			1

LOCATION

Home	30
Other house	3
Business esta	11
Work	5
School	5
Outdoors	5
Church	3
Other	6

DURATION

2-30 minutes	14
1-12 hours:	20
1-6 days:	23
1-3 weeks	13
Months:	3

INTERVAL BETWEEEN EXPOSURE AND SYMPTOMS

Immediate:	20
5-30 minutes	18
1-18 hours:	24
1-2 days:	5

TABLE XIV FINANCIAL IMPACT

Money spent in the last year for the following:

	AVERAGE ADULT	AVERAGE CHILD
Drugs	769.7	3.7
Extracts	532.2	0.0
Travel Expenses	585.0	28.6
Clinics or hospitals	595.0	0.0
Health care personnel	231.0	0.0
Environmental modification	3926.7	4300.0
Other expenses	3808.8	1107.1
TOTAL	$10,448.40	$5,439.40

REFERENCES

1. Coombs R.R.A. and Gell P.G.H. Classification of Allergic Reactions Responsible for Clinical Hypersensitivity and Disease. Chapter 25 pgs. 761-781 in Clinical Aspects of Immunology. Eds Gell P.G.H., Coombs R.R.A., and Lachmann P.J. Blackwell Scientific Publications, Edinburgh 3rd Ed. 1975.

2. Fudenberg H.H., Stites D.P., Caldwell J.L.,Wells J.V. Basic and Clinical Immunology 3rd Edition, Lange 1980.

3. Bardana E. Jr. Office Epidemics. The Sciences 1986: Nov/Dec. 39-44.

4. Acheson E.D. The Clinical Syndrome variously called Benign Myalgic Encephalomyelitis, Iceland Disease and Epidemic Neuromyasthemia. Am. J. Med. 1959; 569-595.

5. Henderson D.A., Shelokov A. Epidemic neuromyasthemia - Clinical Syndrome? N.E.J.M. 1959; 260:757-764; 814-818.

6. Behan P.O. The Post-Viral Fatigue Syndrome - An analysis of the findings in 50 Cases. J. Infect. 1985; 10:211-222.

7. Tobi M. and Straus S.E. Chromic Epstein-Barr Virus Disease. Ann. Int. Med. 1985; 103: 951-955.

8. Tobi M. et.al. Prolonged Atypical Illness Associated with Serological Evidence of Persistent Epstein-Barr Virus Infection. The Lancet 1982; 1:61-69.

9. Jones J.F. et.al. Evidence for Active Epstein-Barr Virus Infection in Patients with Persistent Unexplained Illness: Elevated Anti-Early Antigen Antibodies. Ann. Int. Med. 1985; 102:1-7.

10. Welliver R. C. Editorial. Allergy and the Syndrome of Chronic Epstein-Barr Virus Infecton. J. Allerg. Clin .Immunol. 1986; 78:278-281.

11. Smythe H. "Fibrositis" and other diffuse musculoskeletal Syndromes, pgs. 481-486 Chapter 32 in Textbook of Rheumatology, Eds Kelley et. al., Saunders, Toronto 2nd Ed, 1985.

12. Randolph T.G. The Ecologically - Oriented Medical History. Clinical Ecology 1982; 1:1-13.

13. Bell I.R. Clinical Ecology. A New Medical Approach to Environmental Illness. Common Knowledge Press. Bolinas California 1982.

14. American Academy of Allergy and Immunology. Position Statements:
Clinical Ecology J. All. Clin. Immunol.1986; 78:269-270.
Candidiasis Hypersensitivity Syndrome, ibid 1986; 78:271-272.
Unproven Procedures for Diagnosis and Treatment of Allergic and Immunologic Diseases, ibid 1986; 78:275-277.

15. Terr A.I. Environmental Illness Arch. Int. Med. 1986; 146:145-149.

16. Maclennan J.G. Clinical Titration Principles and Techniques. Part II. Clinical Ecology 1984; 11:207-213.

17. Susser M. Causal Thinking in the Health Sciences. Concepts and Strategies of Epidemiology. Oxford University Press. Toronto 1973.

18. Sackett D.L. Rules of Evidence and Clinical Recommendations of the Use of Anti-thrombotic Agents. Chest 1986; Supplement 89:2S-4S.

19. Thomson G.M. et.al. Report of the Ad Hoc Committee on Environmental Hypersensitivity Disorders to the Ontairo Ministry of Health, August 1985 pgs. 1-312 with appendices.

20. Zimmerman B. Report of the Advisory Panel on Environmental Hypersensitivity to the Ministry of Health, Province of Ontario, September 1986 pgs. 1-19.

21. California Medical Association Scientific Board Task Force on Clinical Ecology: Clinical Ecology - A Critical Appraisal [information] West. J. Med. 1986; 144:239-245.